

**REMARKS**

A. Status of the Claims

Claims 16-21 and 27-40 are pending, with claims 27-30 being withdrawn from consideration. Currently, claims 16-21 and 31-40 are under examination.

Claims 32-40 are rejected under 35 U.S.C. § 101 for allegedly being directed to non-statutory subject matter.

Claims 17-21 and 31 are rejected under 35 U.S.C. § 112, first paragraph, for allegedly containing new matter.

Claim 17 is rejected under 35 U.S.C. § 112, second paragraph, for allegedly being indefinite.

Claims 19-21 are rejected under 35 U.S.C. § 112, first paragraph, for allegedly containing new matter.

Claims 16-21 and 31-40 are rejected under 35 U.S.C. § 112, second paragraph, for allegedly being indefinite.

Claim 20 is objected to for including extra spaces in line 1 of the claim, before and after the limitations “genetically”, “engineered”, and “microorganism”.

B. Rejection of Claims 32-40 Under 35 U.S.C. § 101

The Office Action rejects claims 32-40 as being directed to non-statutory subject matter. Briefly, the Office Action asserts that the claims “fail to distinguish over a pneumolysin nucleic acid molecule having one or more spontaneous mutations therein said nucleic acid molecule comprised within a pneumococcus bacterium as it exists naturally” [Office Action, page 2].

In response thereto, and without agreeing to the propriety of the rejection, Applicants have amended claims 32-40 to recite “a recombinant nucleic acid molecule.” Support for these amendments is found throughout the specification [see specification as filed, page 52, lines 17-20 and Table 6]. Furthermore, it should be noted that independent claims 16 and 17 already recite this limitation, and these claims are not rejected as being directed to non-statutory subject matter. Applicants respectfully submit that this amendment differentiates the claimed invention from a wild-type pneumolysin gene containing one or more spontaneous mutations, and therefore respectfully request that this rejection be withdrawn.

C. Rejection of Claims 17-21 and 31 Under 35 U.S.C. § 112, First Paragraph

The Office Action rejects claim 17 (and its dependent claims 18-21 and 31) for reciting the phrase “non-coding sequence changes thereof,” asserting that this phrase is not supported by the application as originally filed.

Without agreeing to the propriety of the rejection, Applicants have amended claim 17 to instead recite “variants of the nucleic acid sequence of SEQ ID NO: 1, said variants including changes in the nucleic acid sequence of SEQ ID NO: 1 that do not result in a change in the polypeptide encoded by the recombinant nucleic acid molecule.” The originally filed specification describes nucleotide mutations that do not result in a change in the translated amino acid product [see specification, p. 33, line 30 - p. 34, line 4]. As is well known in the art, such mutations are the result of the fact that several different three-nucleotide combinations (*i.e.*, codons) code for the same amino acid. Applicants respectfully submit that claim 17, as amended herein, is supported by the application as originally filed. Applicants respectfully request that this rejection be withdrawn.

D. Rejection of Claim 17 Under 35 U.S.C. § 112, Second Paragraph

The Office Action rejects claim 17 for reciting the phrase “the non-coding sequence changes thereof,” asserting that this phrase is unclear.

As noted above, claim 17 has been amended to recite “variants of the nucleic acid sequence of SEQ ID NO: 1, said variants including changes in the nucleic acid sequence of SEQ ID NO: 1 that do not result in a change in the polypeptide encoded by the recombinant nucleic acid molecule.” The specification describes nucleotide mutations that do not result in a change in the translated amino acid product [e.g., see p. 33, line 30 - p. 34, l. 4] As is well known in the art, such mutations are the result of the fact that several different three-nucleotide combinations (*i.e.*, codons) code for the same amino acid.

In view of this amendment, Applicants respectfully submit that claim 17, as well as corresponding dependent claims 18-21 and 31, are not indefinite, and respectfully request that this rejection be withdrawn.

E. Rejection of Claims 19-21 under 35 U.S.C. § 112, First Paragraph

The Office Action rejects claims 19-21 for reciting the phrase “genetically engineered microorganism or genetically engineered cell,” asserting that the phrase “genetically engineered” lacks support in the application as originally filed.

Without agreeing to the propriety of this rejection, and in the interest of expediting prosecution, Applicants have deleted these phrases from claims 19-21. Claim 19 has been amended, and now recites a “microorganism or cell that has been transformed to comprise the recombinant nucleic acid molecule of any of claims 16-17 or claims 32-40.” As the Office

Action itself concedes, pages 30-33 of the specification describe the transformation of host cells to contain and express modified pneumolysin [see Office Action, page 4, lines 7-10]. Applicants respectfully submit that the claim, as amended, finds support in the application as filed. Accordingly, Applicants request that this rejection be withdrawn.

F. Rejection of Claims 16-21 and 31-40 Under 35  
U.S.C. § 112, Second Paragraph

Regarding claim 20, as per the Examiner's suggestion, Applicants have amended the claim to recite "wherein the ~~genetically engineered~~ microorganism ~~or genetically engineered cell~~ is selected from the group consisting of bacteria[[,]] and yeast, and the cell is selected from the group consisting of mammalian and insect cells." instead of "wherein the genetically engineered microorganism or genetically engineered cell is selected from the group consisting of bacteria, yeast, mammalian and insect cells." In view of this amendment to claim 20, the rejection has been rendered moot.

Regarding claims 32-40, as per the Examiner's suggestion, Applicants have amended the claims to recite "nucleic acid molecule encoding the ~~nucleic acid sequence of~~ modified pneumolysin polypeptide." In view of these amendments, the rejection has been rendered moot.

Regarding claim 16, as per the Examiner's suggestion, Applicants have amended the claim to explicitly recite that the substitutions occur in the sequence of SEQ ID NO: 3. In view of these amendments, the rejection has been rendered moot.

Claims 18-21 and 31 are rejected as being indefinite due to their dependence from claim 16. In view of the above-described amendments, it is respectfully submitted that this rejection has also been rendered moot.

E. Objection to Claim 20

The present Final Office Action objects to claim 20 for including extra spaces between the words of line 1 of claim 20. The appearance of the extra spaces was actually due to the text of the claims previously being justified to both the left and the right. In the present Amendment, the claims are left justified, and the appearance of extra spaces has therefore been removed.

**AUTHORIZATION**

The Commissioner is hereby authorized to charge any additional fees which may be required for consideration of this Amendment to Deposit Account No. **50-3732**, Order No. **13564-105004US3**. In the event that an extension of time is required, or which may be required in addition to that requested in a petition for an extension of time, the Commissioner is requested to grant a petition for that extension of time which is required to make this response timely and is hereby authorized to charge any fee for such an extension of time or credit any overpayment for an extension of time to Deposit Account No. **50-3732**, Order No. 13564-105004.

Respectfully submitted,  
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